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Therapeutic Drug Quantification using Targeted Mass Spectrometry

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Abstract (2000)

Keywords

Biological Treatment, disease modifying anti-rheumatic treatment (DMARD), b biological DMARD (bDMARD), parallel reaction monitoring

Introduction:

Rheumatic diseases involve auto-immune, and inflammatory diseases, in which the inflammatory activity degrades cartilage, and eventually destroys the joints. We have the past five years, systematically reduced treatment frequency and dosage using empirical clinical data and patient

outcome. Previous, determination of the optimal treatment dosage and frequency for biological drugs was based on clinical symptoms and patient questionnaire feedback, with no truly objective biochemical evaluations. Hence, we seek to quantify the biological drug concentrations in the patients to establish a more objective dosing strategy. Previous studies have utilized immuno-based assays, which are sensitive, but limited to availability of good antibodies. They also require high volumes of sample, and are not readily multiplexed. In this study, we developed a parallel reaction monitoring (PRM) based method on four selected biological drugs on a QExactive HF.

Method:

A standard method for ELISA preparation was optimized and scaled down for nUPLC-MS/MS. Four biological drugs and serum samples from patients were immunoprecipitated, and characterized on a Q Exactive high field mass spectrometer. Based on the results, a target list of proteotypic peptides and a spectral database was constructed, and used to establish a PRM method in Skyline, which was utilized to reanalyze the samples.

Results:

We have successfully established a method able to quantify three of the four biological drugs. Interestingly, we show that the PRM method from one commonly administered biological drug, infliximab, also works on the biosimilar version of infliximab with no modifications made to the method used above.

Conclusion:

We have established the foundation for accurately determining the concentration of several biological drugs routinely used in clinical settings. The methods can provide objective measurements to help establish the correct treatment dosage and frequency.